IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Völkel et al.	Docket No.:	52203
Serial No.:	10/076,514	Confirmation No.:	3431
Filing Date:	2/19/2002	Examiner:	YOUNG, MICAH PAUL
Customer No.:	26474	Art Unit:	1618

For: Crystalline choline ascorbate

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

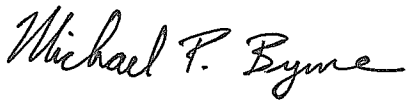
Appeal brief under 37 C.F.R. § 41.37

Sir:

This is an appeal from the Examiner's final rejection of Claims 6, 12, 13 and 23 – 25, dated October 20, 2006. Claims 6, 12, 13 and 23 – 25 are currently pending.

The fee set forth in 37 C.F.R. § 41.20(b)(2) is paid by credit card. Form PTO-2038 is enclosed. Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,
Novak Druce & Quigg, LLP



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Real party in interest:

The real party in interest is BASF Aktiengesellschaft, of Ludwigshafen, Germany.

Related appeals and interferences:

To the best of the undersigned's knowledge, there are no related interferences or judicial proceedings.

Status of claims:

- Claims 6, 12, 13 and 23 – 25 are pending in the application
- Claims 6, 12, 13 and 23 – 25 stand rejected, and are being appealed.
- Claims 1 – 5, 7 – 11, 14 – 22, and 26 are canceled.

Status of amendment:

No amendment was filed subsequent to the final rejection dated October 20, 2006.

Summary of claimed subject matter:

The claimed invention relates to methods for preparing crystalline choline ascorbate[1] of a purity and stability sufficient for use in the food and pharmaceutical sectors, for example as an additive in an animal feeds or as an additive to multivitamin tablets.

The independent claims involved in the appeal are claims 6 and 23. All other claims depend either from claim 6 or from claim 23. Summary of the subject matter of the dependent claims is omitted as unnecessary.

Claim 6 is directed to a single-step process for preparing crystalline choline

[1] Choline acts as an important factor in biochemical process. For example, a deficiency of choline in animals leads to the formation of a fatty liver. Ascorbic acid is better known as vitamin C.

ascorbate, which comprises reacting ascorbic acid with trimethylamine and ethylene oxide.[2] This single-step reaction is carried out in a temperature range of from 0°C to 5°C[3] in the presence of a water-miscible organic solvent or in the presence of a mixture of water and a water-miscible organic solvent.[4]

Claim 23 is directed to a process for preparing choline ascorbate, comprising three steps: (a) providing a mixture of ascorbic acid, trimethylamine and a solvent, (b) adding to the mixture gaseous ethylene oxide,[5] and (c) crystallizing the choline ascorbate.[6] In the claimed process, stages (a) and (b) are carried out at a temperature of from 0°C to 5°C, [7] and the solvent is a water miscible organic solvent or is a mixture of said organic solvent and water.[8] Moreover, the claim requires the choline ascorbate to be obtained in the form of anhydrous crystals having diffraction lines at d = 3.80 Å and 4.55 Å,[9] and having diffraction lines which are most intense in a range between 3.40 and 4.70 Å, in a 2 T X-ray powder diffractogram, [10] and having a melting point from 123.5 to 124.4°C or in the range from 123.5 to 124.4°C.[11]

Grounds of rejection to be reviewed on appeal

Whether the examiner erred in rejecting claims 6, 12, 13 and 23 – 25 under 35 U.S.C. §103(a) over **Klein et al.** (US 2,870,198) in view of **Spires** (US 4,394,377).

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[2] Specification, page 2, indicated lines 39 - 41.
[3] Example 1, Specification, page 4, indicated lines 25 – 28; Example 2, Specification, page 4, indicated line 45 – page 5, indicated line 1; Example 3, page 5, indicated lines 11 – 15.
[4] Specification, page 2, indicated line 45 – page 3, indicated line 2.
[5] Example 1, Specification, page 4, indicated lines 25 – 28; Example 2, Specification, page 4, indicated line 45 – page 5, indicated line 1; Example 3, page 5, indicated lines 11 – 15.
[6] Specification, page 3, indicated lines 19 – 21.
[7] Example 1, Specification, page 4, indicated lines 25 – 28; Example 2, Specification, page 4, indicated line 45 – page 5, indicated line 1; Example 3, page 5, indicated lines 11 – 15.
[8] Specification, page 3, indicated lines 24 – 25.
[9] Specification, page 2, indicated lines 5 – 7.
[10] Specification, page 2, indicated lines 1 – 3.
[11] Specification, page 4, indicated line 34.

Argument

The examiner erred in rejecting claims 6, 12, 13 and 23 – 25 under 35 U.S.C. §103(a) over Klein et al. (US 2,870,198) in view of Spires (US 4,394,377). This combination fails to teach or suggest all of the claim limitations, and is based on an erroneous reading of Klein et al.

The examiner alleges that the Klein et al. "patent discloses a method of making crystalline choline salts comprising reacting trimethylamine, gaseous ethylene oxide and anhydrous acids at temperatures from 0 – 5 °C …." This allegation is erroneous. In fact, the method actually disclosed by Klein et al. bears little resemblance to the examiner's allegation. Moreover, reading the Klein et al. reference in view of the Spires reference does not result in a combination that teaches or suggests all of the claim limitations.

Appellants respectfully submit that the examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103. When applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to: (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) Reasonable expectation of success is the standard with which obviousness is determined.[12] Moreover, "[t]o establish a *prima facie* case of obviousness the references when combined must teach or suggest all the claim limitations."[13]

The Examiner has not set forth a *prima facie* case of obviousness with regard to the invention of claim 6 as a whole, or with regard to claim 23 as a whole because: The proposed combination results in a multi-step process, not the single step process of claim 6. The proposed combination would not result in a process, as claimed in claim 6, wherein trimethylamine and ethylene oxide are reacted in the presence of an acid. The proposed combination would not result in a process, as claimed in claim 23, wherein gaseous ethylene oxide is added to a mixture of ascorbic acid, trimethylamine and a solvent. The proposed combination would result in a process wherein the reaction

[12] *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).
[13] MPEP §2143.

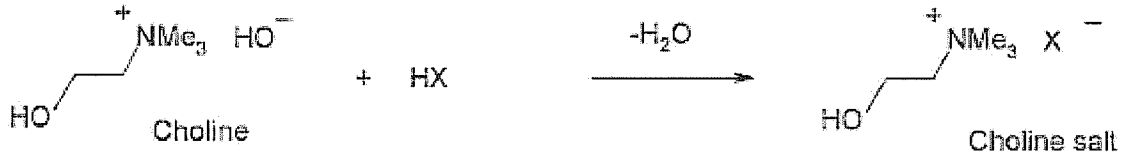
temperature exceeds 5°C. Finally, the proposed combination would result in the production of a heavy viscous oil, instead of producing crystalline choline ascorbate.

These issues will be addressed one at a time, because a *prima facie* case of obviousness cannot be established if the cited reference fails to teach or suggest any one of the claim limitations, however, it is important to bear in mind that the claimed invention must be considered as a whole. Indeed, this invention is greater than the sum of its parts.

The proposed combination results in a multi-step process, not the single step process of claim 6.

Klein et al. disclose a first step of reacting ethylene oxide, trimethylamine and water to completion.[14] This first step is represented below:

Klein et al. disclose a second step of adding a "hot alcoholic solution of [a particular] acid."[15] This second step is represented below:



Klein et al. also disclose a third step, wherein "[the] reaction mixture is cooled to about 5°C, or below."

Spires merely states that "Choline ascorbate can be prepared from choline and ascorbic acid in methanol according to the procedure set out in U.S. Pat. No.

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[14] See: Column 1, indicated lines 35 – 37; Column 2, l indicated lines 45 – 50; Column 2, indicated lines 60 – 65; Column 2, indicated lines 65 – 72; Example 1: Column 3, indicated lines 45 – 52; Example 2: Column 3, indicated line 74 – Column 4, indicated line 7; and Example 3: Column 3, indicated lines 19 – 26.

[15] Klein et al. (US 2,870,198) at column 3, indicated line 35.

2,823,166."[16] In other words, Spires, at best, contemplates the production of choline ascorbate according to the second step disclosed in Klein et al. Thus, Spires provides no teaching, suggestion or motivation to modify the multi-step process of Klein et al. to produce crystalline choline ascorbate in a single-step by reacting ascorbic acid with trimethylamine and ethylene oxide, as claimed in claim 6.

For this reason alone, the examiner has failed to establish a *prima facie* case of obviousness with regard to independent claim 6. In order "[t]o establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim limitations."[17] Since the proposed combination does not teach or suggest a single-step process, the proposed combination does not teach or suggest all the limitations of claim 6. For at least these reasons, claim 6 is unobvious over Klein et al. in view of Spires.

The proposed combination would not result in a process, as claimed in claim 6, wherein trimethylamine and ethylene oxide are reacted in the presence of an acid.

As discussed above, Klein et al. disclose a first step of reacting ethylene oxide, trimethylamine and water to completion,[18] and a second step of adding a "hot alcoholic solution of [a particular] acid."[19] At best, Spires contemplates the production of choline ascorbate according to the second step disclosed in Klein et al. Thus, it should be clear that the proposed combination does not teach or suggest a process, as claimed in claim 6, wherein trimethylamine and ethylene oxide are reacted in the presence of an acid.

Again, in order "[t]o establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim limitations."[20] Since the proposed combination does not teach or suggest a process wherein trimethylamine and

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[16] US 4,394,377, column 4, indicated lines 10 – 13.

[17] MPEP §2143.

[18] See: Column 1, indicated lines 35 – 37; Column 2, l indicated lines 45 – 50; Column 2, indicated lines 60 – 65; Column 2, indicated lines 65 – 72; Example 1: Column 3, indicated lines 45 – 52; Example 2: Column 3, indicated line 74 – Column 4, indicated line 7; and Example 3: Column 3, indicated lines 19 – 26.

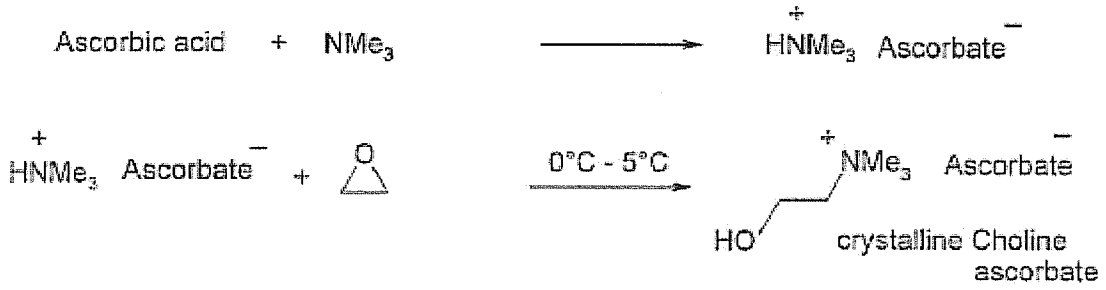
[19] Klein et al. (US 2,870,198) at column 3, indicated line 35.

[20] MPEP §2143.

ethylene oxide are reacted in the presence of an acid, the proposed combination does not teach or suggest all the limitations of claim 6. For at least these reasons, claim 6 is unobvious over Klein et al. in view of Spires

The proposed combination would not result in a process, as claimed in claim 23, wherein gaseous ethylene oxide is added to a mixture of ascorbic acid, trimethylamine and a solvent.

Again, Klein et al. discloses reacting ethylene oxide, trimethylamine and water to completion,[21] and subsequently adding a "hot alcoholic solution of [a particular] acid."[22] At best, Spires contemplates the production of choline ascorbate according to the second step disclosed in Klein et al. Thus, it should be clear that the proposed combination does not teach or suggest a process, as claimed in claim 23, which requires "providing a mixture of ascorbic acid, trimethylamine and a solvent, [and] adding to the mixture gaseous ethylene oxide...." The process of claim 23 is represented below:



Again, in order "[t]o establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim limitations."[23] Since the proposed combination does not teach or suggest a process wherein gaseous ethylene oxide is added to a mixture of ascorbic acid, trimethylamine and a solvent, the proposed combination does not teach or suggest all the limitations of claim 23. For at least these reasons, claim 23 is unobvious over Klein et al. in view of Spires.

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[21] See: Column 1, indicated lines 35 – 37; Column 2, l indicated lines 45 – 50; Column 2, indicated lines 60 – 65; Column 2, indicated lines 65 – 72; Example 1: Column 3, indicated lines 45 – 52; Example 2: Column 3, indicated line 74 – Column 4, indicated line 7; and Example 3: Column 3, indicated lines 19 – 26.

[22] Klein et al. (US 2,870,198) at column 3, indicated line 35.

[23] MPEP §2143.

The proposed combination would result in a process wherein the reaction temperature exceeds 5°C.

Claim 6 requires the reaction of ascorbic acid with trimethylamine and ethylene oxide to be carried out in a temperature range of from 0°C to 5°C. Claim 23 requires steps (a) and (b) wherein gaseous ethylene oxide is added to a mixture of ascorbic acid, trimethylamine and a solvent to be carried out at a temperature of from 0°C to 5°C.

As discussed above, the proposed combination does not teach or suggest a process, as claimed in claim 6, wherein trimethylamine and ethylene oxide are reacted in the presence of an acid. Nor does the proposed combination teach or suggest a process, as claimed in claim 23, wherein gaseous ethylene oxide is added to a mixture of ascorbic acid, trimethylamine and a solvent. The proposed combination would result in a completely different process. Thus, it should not be surprising that the proposed combination does not teach or suggest the required temperature range of from 0°C to 5°C.

As has been discussed, Spires, at best, contemplates the production of choline ascorbate according to the second step disclosed in Klein et al. In the first step disclosed by Klein et al. trimethylamine and ethylene oxide are reacted to completion in a temperature range of from 0°C to 100°C[24] Example 1 discloses that this step was conducted at "a temperature of about 0°C to 10°C."[25] Example 2 discloses that this step was conducted "at a temperature of 15°C - 20°C."[26] Example 3 discloses that this step was conducted "at a temperature of 16°C - 30°C."[27] Thus, even at this point, it should be clear that the proposed combination does not teach or suggest the required temperature range of from 0°C to 5°C. Yet, Klein et al. also disclose a second step, wherein a hot alcoholic solution of an acid is added. Klein et al. disclose that "if desired ... [this hot alcoholic solution of the acid] may be prepared using an alcohol which has been heated to or near its reflux temperature in order to give a higher concentration of the acid in the

[24] Klein et al. (US 2,870,198) at column 2, indicated lines 50 – 55.
[25] Klein et al. (US 2,870,198) at column 3, indicated lines 50 – 53.
[26] Klein et al. (US 2,870,198) at column 4, indicated lines 3 – 4.
[27] Klein et al. (US 2,870,198) at column 4, indicated lines 23 – 24.

solvent."[28] Klein et al. discloses that when this "hot alcoholic solution of the acid" is added to the mixture obtained as a product of the reaction in the first step, the temperature of the overall mixture rises. Klein et al. does not specify precisely how high the temperature rises, however, it seems clear that the temperature rises higher than 5°C, because Klein et al. disclose a third step, wherein "[the] reaction mixture is cooled to about 5°C, or below." Moreover, in Example 1 of Klein et al., it is noted that "[t]his mixture was … cooled with agitation to 5°C."[29]

Again, in order "[t]o establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim limitations."[30] Since the proposed combination does not teach or suggest the required temperature range of from 0°C to 5°C., the proposed combination does not teach or suggest all the limitations of claim 6 or of claim 23. For at least these reasons, claim 6 and claim 23 are unobvious over Klein et al. in view of Spires.

The proposed combination would result in the production of a heavy viscous oil, instead of producing crystalline choline ascorbate.

As mentioned above, Spires states that "Choline ascorbate can be prepared from choline and ascorbic acid in methanol according to the procedure set out in U.S. Pat. No. 2,823,166."[31] This reference (hereinafter, Hoffmann) discloses a process substantially identical to the process of Klein et al. Since the process of Hoffmann is substantially identical to the process of Klein et al., it is reasonable and appropriate to look to Hoffmann to ascertain additional details regarding what would be produced by the process according to the examiner's proposed combination. A review of Hoffmann reveals that the process according to the examiner's proposed combination would not result in the production of crystalline choline ascorbate, but in the production of a heavy viscous oil.[32]

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[28] Klein et al. (US 2,870,198) at column 3, indicated lines 15 – 20.
[29] US 2,870,198, column 3, indicated lines 54 – 55.
[30] MPEP §2143.
[31] US 4,394,377, column 4, indicated lines 10 – 13.
[32] US 2,823,166, column 3, indicated line 55.

Since the proposed combination does not teach or suggest a process wherein crystalline choline ascorbate is prepared, the proposed combination does not teach or suggest all the limitations of claim 6 or of claim 23. For at least these reasons, claim 6 and claim 23 are unobvious over Klein et al. in view of Spires.

Finally, it is noted that "[i]f an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious."[33] Thus, claims 12 and 13, which depend from claim 6 are nonobvious, and claims 24 – 25, which depend from claim 23 are nonobvious.

[33] MPEP §2143.03, citing *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claims appendix.

1 – 5. (canceled)

6. (previously presented) A process for preparing crystalline choline ascorbate, which comprises reacting ascorbic acid with trimethylamine and ethylene oxide, and carrying out the reaction in a temperature range from 0°C to 5°C in the presence of a water-miscible organic solvent or in the presence of a mixture of water and a water-miscible organic solvent.

7 – 11. (canceled)

12. (previously presented) The process of claim 6, wherein ascorbic acid is reacted with trimethylamine and ethylene oxide by adding ethylene oxide to a mixture comprising the ascorbic acid and the trimethylamine.

13. (previously presented) The process of claim 12, wherein gaseous ethylene oxide is added to the mixture comprising the ascorbic acid and the trimethylamine.

14 – 22 . (canceled)

23. (previously presented) A process for preparing choline ascorbate, wherein the choline ascorbate is obtained in form of anhydrous crystals having diffraction lines at d = 3.80 Å and 4.55 Å, and having diffraction lines which are most intense in a range between 3.40 and 4.70 Å, in a 2 T X-ray powder diffractogram and having a melting point from 123.5 to 124.4°C or in the range from 123.5 to 124.4°C, which process comprises

   a) providing a mixture of ascorbic acid, trimethylamine and a solvent,
   b) adding to the mixture gaseous ethylene oxide, and
   c) crystallizing the choline ascorbate,

wherein stages (a) and (b) are carried out at a temperature of from 0°C to 5°C, and the solvent is a water miscible organic solvent or is a mixture of said organic solvent and

water.

24. (previously presented) The process of Claim 23, wherein the solvent is a water miscible organic solvent.

25. (previously presented) The process of Claim 23, wherein the choline ascorbate is crystallized from the solvent employed in stage (a).

26. (canceled)

Evidence appendix

None.

Related proceedings appendix

None.